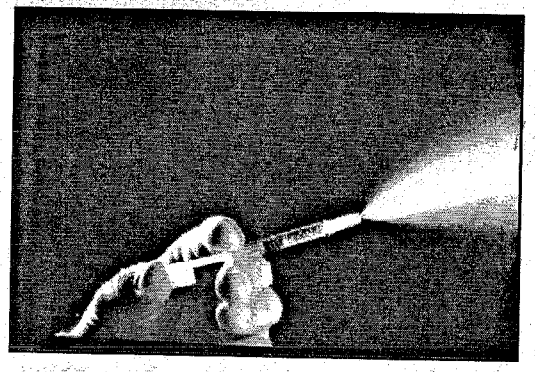
Aviron



FluMist

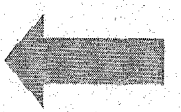
An Influenza Vaccine For Use in Healthy Adults Age 18 – 64

Safety in Adults

Paul M. Mendelman, MD
Aviron

Historical Experience with CAIV Prior to Aviron Clinical Trials

Population	Number Enrolled
Children	2743
Adults	5348
Total (All Ages)	8091



- Primarily monovalent or bivalent formulations

Conclusion: CAIV was safe and well-tolerated

Adults Vaccinated with FluMist

Aviron Experience

All Adults

Population	Healthy	High Risk
18 – 64 Years	3947	65[a]
Adults with COPD (mean age 68)	—	1107
65 and older	—	131
Total	3947	1303

[a] 37 adults with asthma and 28 adults infected with HIV

Conclusion: 5,250 adults vaccinated with FluMist

Collection of Safety Data

Aviron Trials

- **Methods**
  - Diary card
  - Monitoring of medical records
  - Telephone calls to participants
- **Types**
  - Serious adverse events (Day 0 to Day 28)
  - Post-vaccination reactogenicity period (Day 0 to Day 7)
    - Reactogenicity events (pre-specified)
    - Other adverse events (not pre-specified)
    - Medication use

Serious Adverse Events (SAEs) In Adults

Adults

Population	FluMist # SAEs / # Enrolled (%)	Placebo # SAEs / # Enrolled (%)
18 – 64 Year Olds		
Healthy (proposed indication)	38 / 3947 (1%)	24 / 1646 (1.4%)
Asthma	0 / 37 (0%)	0 / 13 (0%)
HIV-infected	0 / 28 (0%)	1 / 29 (0%)
≥ 65 Years of Age	2 / 131 (1.5%)	2 / 101 (1.9%)
Adults with COPD	290 / 1107 (26%)	319 / 1108 (29%)

Placebo used was allantoic fluid

Conclusion: SAEs were balanced between FluMist and placebo recipients

All Cause Mortality in Adults

Adults

- One death in a healthy adult
  - Accidental drowning/alcohol intoxication
    - 16 days after FluMist
- 64 deaths in adults with COPD in VA trial
  - All received TIV on the same day
  - 34 in FluMist recipients (3.1%)
    - 3 within 28 days
    - 1 vaccine related (218 days after vaccination)
  - 30 in placebo recipients (2.7%)
    - 5 within 28 days
    - 3 vaccine related (3, 78, & 158 days after vaccination)

Vaccine Related Serious Adverse Events (SAEs)

Adults

- None in healthy adults
- 31 in adults with COPD in the VA Trial
  - 9 in 1,107 vaccines (0.8%)
  - 22 in 1,108 placebo recipients (2%)

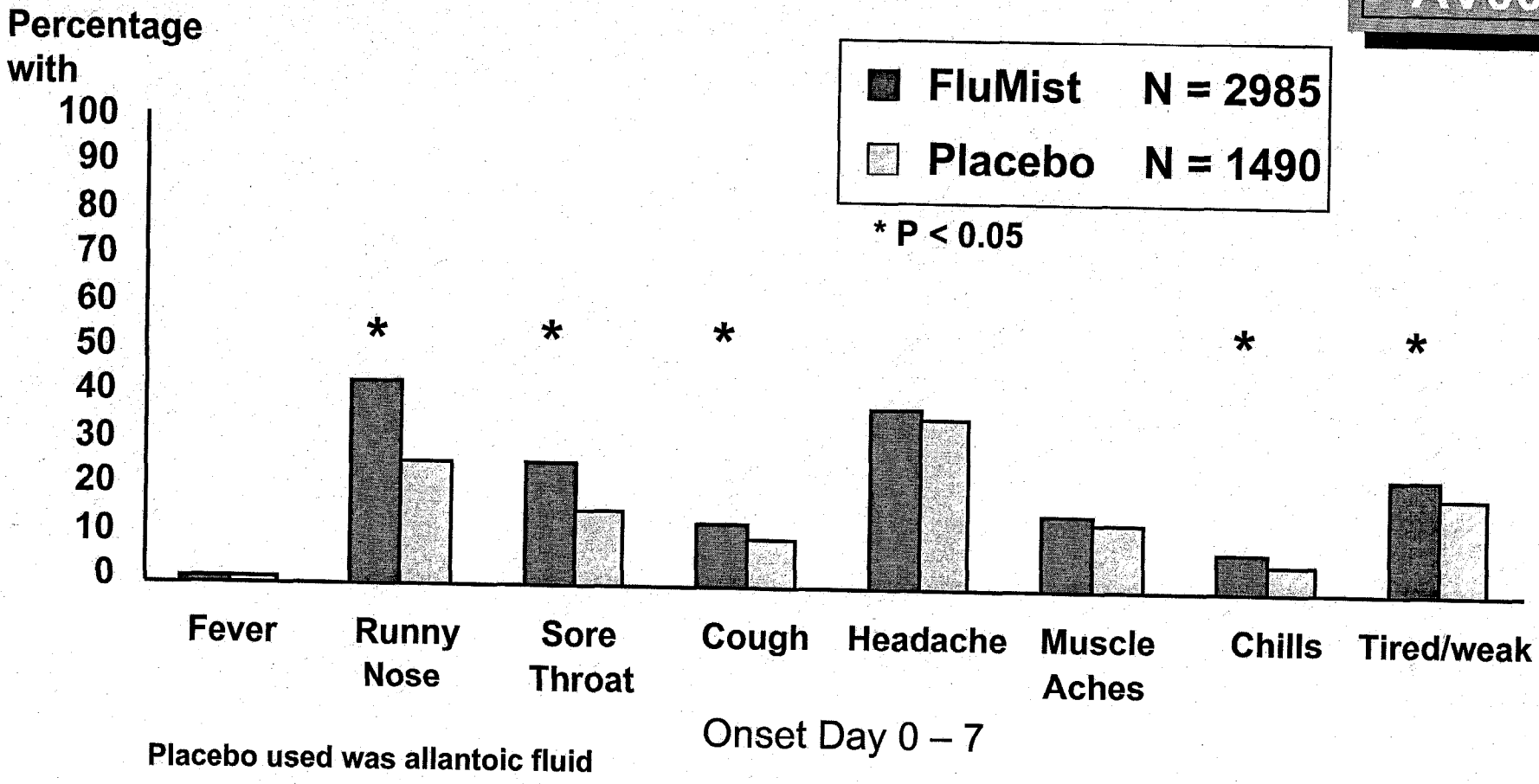
Demographic Characteristics of Healthy Adults in Study AV009

Healthy Adults Study AV009

Characteristics	FluMist N = 3041	Placebo N = 1520
Age in Years		
Median/Mean	38	38
Gender		
Female	55%	54%
Race/Ethnicity		
White	85%	84%
Black	10%	11%
Hispanic	2%	2%
Asian	2%	2%
Other	1%	1%

Adults with Reactogenicity Events

Healthy Adults Study AV009

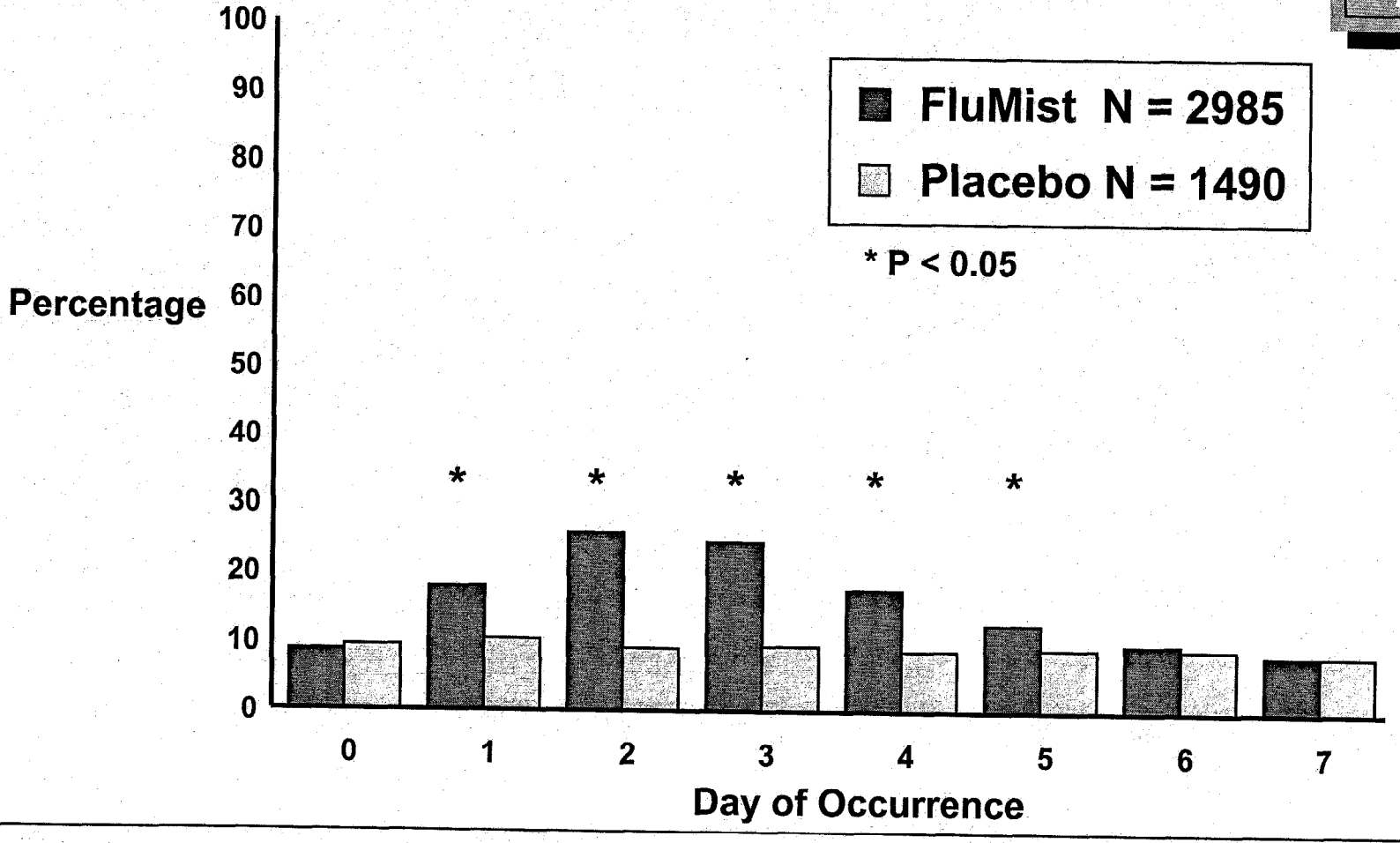


Placebo used was allantoic fluid

Conclusion: Several reactogenicity events were significantly increased after vaccine administration

Adults with Runny Nose Day of Occurrence Analysis

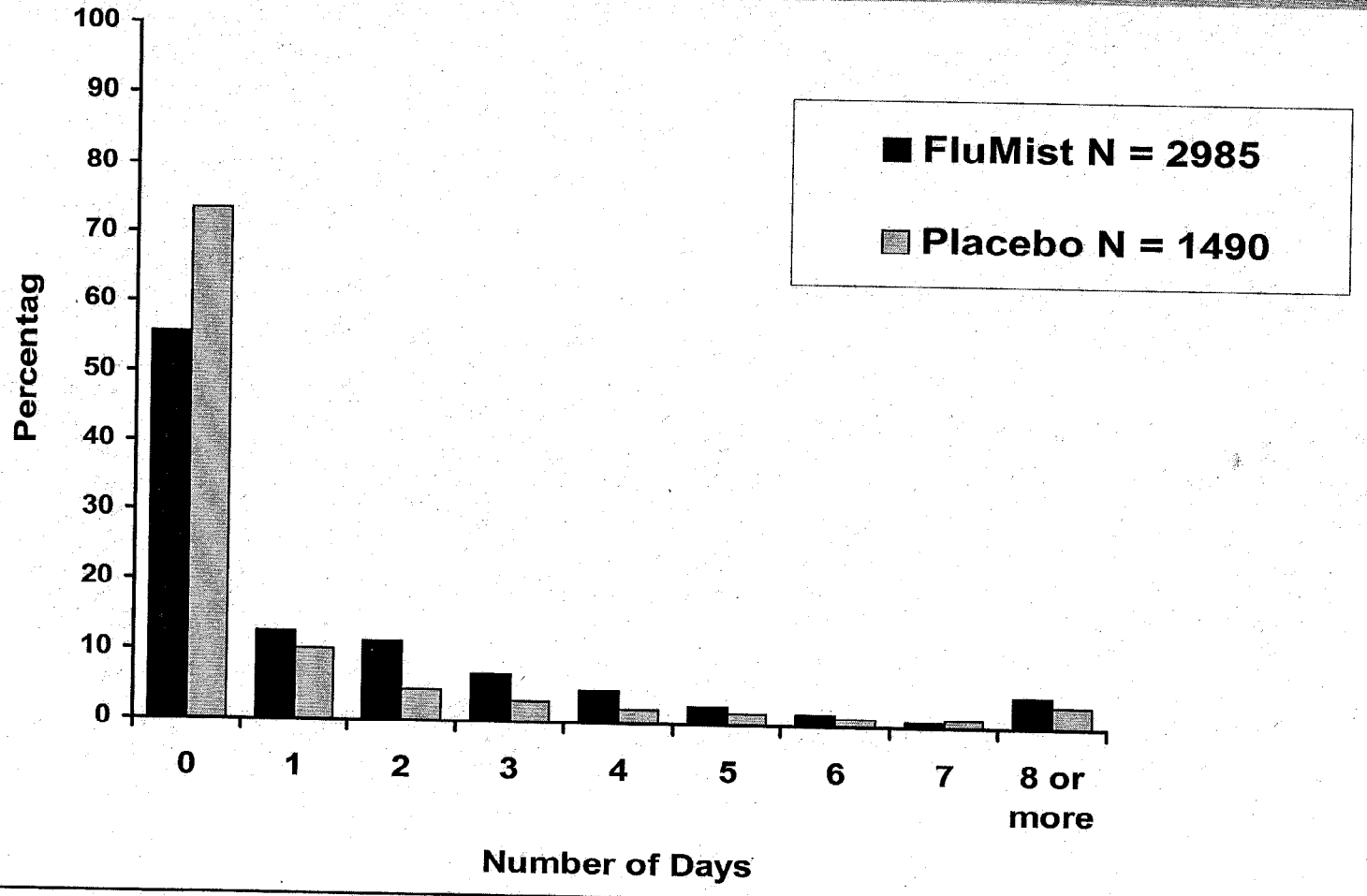
Healthy Adults Study AV009



Conclusion: Runny nose was significantly increased on multiple days after vaccine administration

Adults
Number of Days with Runny Nose

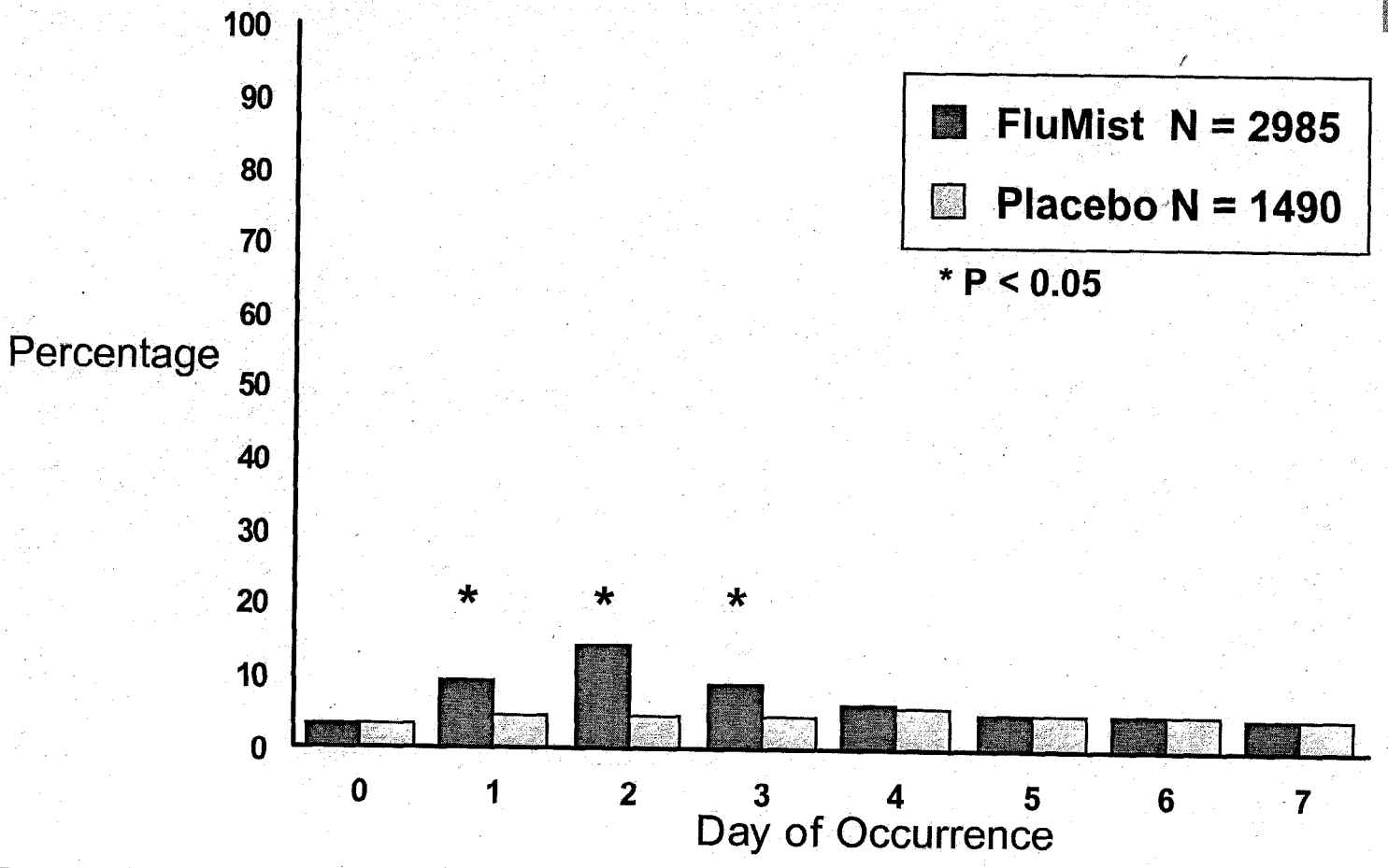
Healthy Adults Study AV009



Conclusion: Most vaccinees had no days of runny nose. However, more placebo recipients had no days of runny nose.

Adults with Sore Throat Day of Occurrence Analysis

Healthy Adults Study AV009



Conclusion: Sore throat was significantly increased on Days 1, 2, and 3 after vaccine administration

Healthy Adults with Illness in 7 Day Post-Vaccination Period

Healthy Adults Study AV009

Participants with	FluMist N = 2985	Placebo N = 1490	P Value
CDC-ILI[a]	1.1%	0.8%	0.43
Temperature > 100° F	1.3%	1.3%	1.0

[a] CDC-ILI defined as temperature ≥ 100°F with cough or sore throat events on same day or on consecutive days

Conclusion: FluMist was not significantly associated with fever or influenza-like illness in healthy adults

Adults with Medication Use Onset Day 0 – 7

Medication	FluMist N = 3041	Placebo N = 1520	P Val
Antibiotics - oral	1.6%	1.1%	0.2
Analgesics/antipyretics	26.1%	23.9%	0.1
Antihistamines/antitussives/ decongestants	9.0%	8.0%	0.2
Beta Agonist/Glucocorticoids (Nasal/oral)	1.2%	1.6%	0.4

* Fisher's Exact Test

Conclusion: FluMist was not significantly associated with in medication use

Selected Events in Healthy Adults During the Reactogenicity Period

Healthy Adults Placebo Controlled Trials 18-64 Years

Event	FluMist N = 3287	Placebo N = 1632	P Value*
	N (%)	N (%)	
Conjunctivitis	5 (0.2)	6 (0.4)	.20
Abdominal Pain	25 (0.8)	18 (1.1)	.25
Lower Respiratory Illness	39 (1.2)	15 (0.9)	1.00
Asthma/Wheezing	2 (0.1)	1 (0.1)	.47
Pneumonia	1 (<0.1)	0 (0)	1.00
Otitis Media	1 (<0.1)	1 (0.1)	.55

Safety Conclusions

Healthy Adults

- FluMist was safe and well-tolerated in healthy adults 18 - 64 years of age
- 3,947 healthy adults have received FluMist
- Mild, self-limited reactogenicity events observed
- Low risk of other adverse events